Cerebral neuromagnetic responses evoked by two-channel bone-conducted ultrasonic stimuli

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1 Introduction

Ultrasound, whose frequency is over 20 kHz, is not a sound mainly to hear in general use. However, in 1948, Gavreau has reported that it could be perceived as sound when stimulated by bone conduction [1]. There are some interesting characteristics of bone-conducted ultrasound that are quite different from those of audible sound, those are presumed to occur due to the difference of the mechanism of the hearing. However, the mechanism of ultrasonic hearing is not completely made clear and there has been a controversy over it. One predicts that the certain biomechanical demodulation transform ultrasound into low frequency audible sound [2], and others hypothesize contribution of the cochlear hair cells [3, 4, 5], or the vestibular hair cells [6, 7]. To provide conclusive evidence relevant to the debate mentioned above, we had measured with magnetoencephalography (MEG) and positron emission tomography (PET) to elucidate the mechanism of ultrasonic hearing and revealed the cortical areas activated by bone-conducted ultrasonic stimuli [8, 9]. In this study, we measured with MEG for two-channel bone-conducted ultrasonic stimuli to shed light on the areas that were remained unclear.

2 Methods

2.1 Subjects

Six healthy volunteers (age range 22-27 years; all males; five right-handed) with no history of hearing deficits participated in the experiment. Voluntary consent was obtained from the subjects prior to participation. During the recordings, subjects were seated underneath the neuromagnetometer (Neuromag-122™) and were instructed to ignore the tones presented, to keep the eye fixation still, and to avoid excessive eye movements and blinks.

2.2 Stimulator

Ultrasonic stimuli (25-55 kHz) were produced by two independent function generators (AFG320, Sony/Tektronix Corp.) and were presented on the both left and right sternocleidomastoid muscle with two independent ceramic transducers (Murata Manufacturing Co., Ltd.). 2 kHz stimuli were also produced by the generators and presented by the transducers.

2.3 Stimuli

The stimuli presented to the subjects consisted of two types of tones, ultrasonic stimuli (10 ms plateau, 10 ms rise/fall) and 2 kHz stimuli (10 ms plateau, 10 ms rise/fall) for control experiment. Furthermore, both stimuli consisted of two types: a standard stimulus ($p = 0.9$) and a deviant stimulus ($p = 0.1$). Therefore, subjects were presented with a total of four types of stimulus patterns: 1) ultrasonic stimuli at left sternocleidomastoid muscle as deviant and ultrasonic stimuli at right sternocleidomastoid muscle as standard, 2) ultrasonic stimuli at left sternocleidomastoid muscle as standard and ultrasonic stimuli at right sternocleidomastoid muscle as deviant, 3) 2 kHz stimuli at left sternocleidomastoid muscle as deviant and 2 kHz stimuli at right sternocleidomastoid muscle as standard, 4) 2 kHz stimuli at left sternocleidomastoid muscle as standard and 2 kHz stimuli at right sternocleidomastoid muscle as deviant. The deviants differed from the standards in its location of the transducer, left or right sternocleidomastoid (Figure 1). Stimuli were delivered in random order to the subjects with an inter stimulus interval of 700 ms. Before starting the main experiment, each subject was presented 25 to 55 kHz stimuli by 1 kHz step with the ceramic transducer and were instructed to state the frequency of the stimuli that they perceived most loudly. This was to determine the unique frequency of the ultrasonic experiment for each of the subject. The amplitude for those ultrasonic stimuli was determined for each subject so as to become the most clearly perceiving (MCP) level. The amplitude for 2 kHz stimuli were also determined for each subject to be perceived as equal loudness to the 30-40 dB stimuli, which we defined as a reference value, given by the bone-conduction stimulator (Audiometer AA67, Rion Co., Ltd.). Both ultrasonic and 2 kHz stimuli were delivered to the left and right sternocleidomastoid muscle with the transducer and were adjusted so as the direction of the perceived sound image produced by the given stimuli would be the same side of the location of the transducer, left and right respectively.

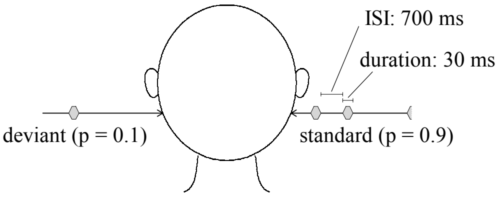

Figure 1: *Illustration of stimulus presentation.*

2.4 Recordings

The experiments were carried out in a magnetically shielded room with a whole-scalp Neuromag-122™ neuromagnetometer, which consists of 122 planar first-order SQUID gradiometers, placed at 61 measurements sites. These gradiometers measure the longitudinal and latitudinal derivatives of B_z, the magnetic field component perpendicular to the surface of the helmet. MEG signals were measured, having been digitized at 400 Hz, and were band-pass filtered through 0.03 to 100 Hz and more than 120 responses were averaged on-line with respect to the onset of the stimuli. The analysis period for the averaged epochs was 500 ms including a 100 ms pre-stimulus baseline. Averaged data were band-pass filtered through 0.1 to 30 Hz off-line. Vertical electrooculogram (EOG) was monitored to reject epochs happened together with signals due to vertical eye movements or blinks (EOG > 150 μV). Epochs containing greater than 3000 fT/cm changes were also rejected. The anatomical T1-weighted MR images were measured with MRI system (AIRIS-II, Hitachi Medical Corp.). Before each recording, the locations of the head position indicator's (HPI) coils, fixed on the scalp of the subjects, were determined with a 3-D digitizer (Isotrack, Polhemus Inc.) to allow alignment of the MEG and MRI coordinating systems.

2.5 Analysis

We determined the amplitude of the response signals as A.

$$A = \sqrt{\left(\frac{\partial B_z}{\partial x}\right)^2 + \left(\frac{\partial B_z}{\partial y}\right)^2} \tag{1}$$

For the responses of the standards and the deviants, both the peaks, that showed the highest amplitude, and their onset latencies were measured. Single equivalent current dipoles (ECDs) were found separately for the left and right hemisphere data during the response peaks. A spherical head model was used in the dipole fitting. We standardized the magnitude of the dipole moments of the ECDs and defined those as the intensity of the activities against the given stimuli. Possible differences in the peak latencies and in the intensity of the activities between the stimulus types were determined with ANOVAs.

3 Results

Figure 2 shows the evoked magnetic fields, measured from the temporal channel, to the deviants and to the standards for 2 kHz bone-conducted stimuli and 32 kHz, which was his fit frequency determined prior to the measurement, ultrasonic stimuli for subject 1. Responses to the deviants and to the standards both showed the maximum amplitude at 68-250 ms.

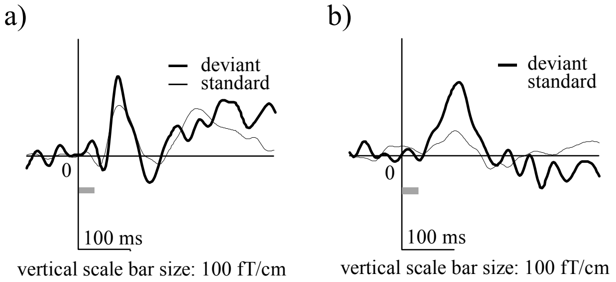

Figure 2: *Averaged responses to the deviants (continuous line) and to the standards (dotted line) for a) 2 kHz bone-conducted stimuli and b) 32 kHz bone-conducted ultrasonic stimuli for subject 1.*

All of the ECDs estimated at those peaks latencies were located on the auditory area (Figure 3). Figure 4a shows the mean peak latencies for the 2 kHz and for the ultrasonic stimuli. The mean peak latencies for the ultrasonic stimuli were significantly later than those of the 2 kHz stimuli ($p < 0.01$). The mean peak latencies for the deviants were significantly later than those of the standards ($p < 0.05$).

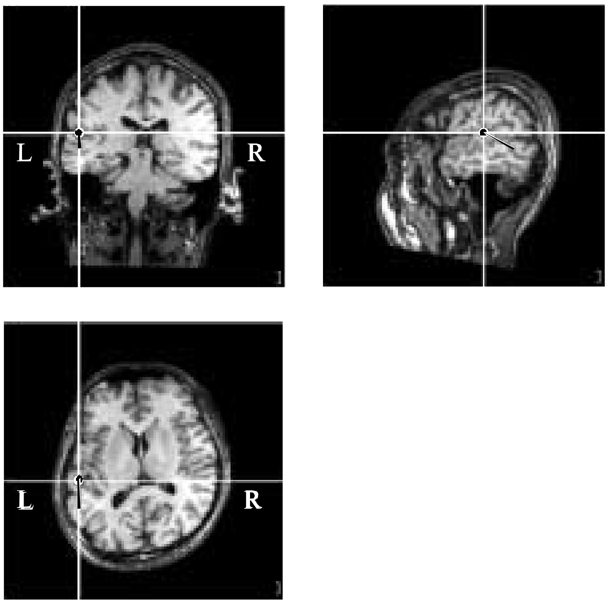

Figure 3: *Equivalent current dipole estimated at the peak latency measured for the standard stimuli superimposed on his magnetic resonance images.*

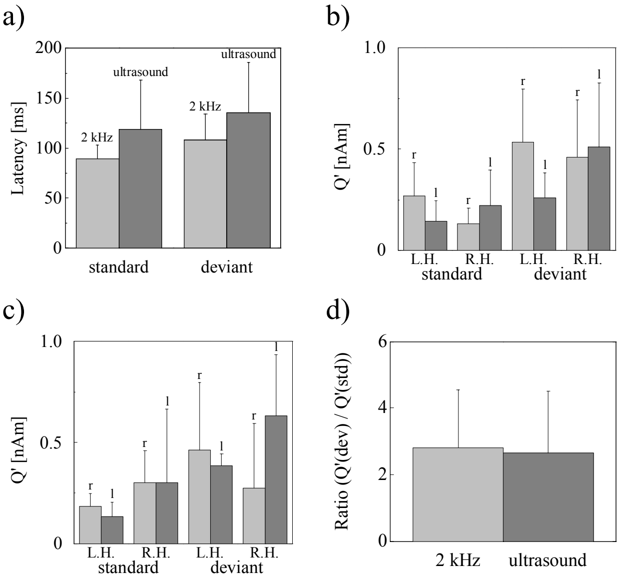

Figure 4: *a) Mean peak latency of the standards and the deviants for 2 kHz bone-conducted stimuli and for ultrasonic bone-conducted stimuli. Standardized mean intensity Q' of the activity for the standards and for the deviants for b) 2 kHz bone-conducted stimuli and for c) ultrasonic bone-conducted stimuli. (L.H.: left hemisphere. R.H.: right hemisphere. l: stimuli were presented to the left sternocleidomastoid muscle. r: stimuli were presented to the right sternocleidomastoid muscle.) d) Ratios of the standardized mean intensity of the activity for the deviants to the standards for 2 kHz bone-conducted stimuli and ultrasonic bone-conducted stimuli.*

Figure 4b shows the standardized mean intensity *Q'* of the activities for the 2kHz bone-conducted stimuli. For the 2kHz stimuli, the standardized mean intensity of the activities for the deviants were significantly larger than that of the standards ($p < 0.001$), and the standardized mean intensity of the activities in the hemisphere contralateral to the stimulated side, left or right, were significantly larger than that of the ipsilateral side ($p < 0.05$), right or left. Figure 4c shows the standardized mean intensity *Q'* of the activities for the ultrasonic bone-conducted stimuli. For the ultrasonic stimuli, the standardized mean intensity of the activities for the deviants were significantly larger than that of the standards ($p < 0.05$), and the standardized mean intensity of the activities in the hemisphere contralateral to the stimulated side were tended to be larger than that of the ipsilateral side, however, no significant difference was observed. Figure 4d shows the ratios of the standardized mean intensity of the activity for the deviants to the standards for 2 kHz bone-conducted stimuli and ultrasonic bone-conducted stimuli, and no significant difference was observed between the ratios of the 2 kHz stimuli and the ultrasonic stimuli.

4 Discussion

Although it is generally said to be difficult to discriminate the sound location for audible bone-conducted sound, the amplitude of the magnetic field evoked for the deviants was significantly larger than that of the standards for 2 kHz stimuli. The result suggests that when stimulated by two different locations, just as like done in this study, it is possible to differentiate those two stimuli even though presented via bone conduction. Correspondingly, differentiation of the deviants and the standards were possible for ultrasonic bone-conducted stimuli, suggests that the sound information of the ultrasonic stimuli will get into the auditory pathway before superior olivary complex.

The latencies of both the deviants and the standards for ultrasonic stimuli were significantly later than those for 2 kHz stimuli. The results raise the possibility of 1) existence of different pathways for the perception of bone-conducted audible sound and bone-conducted ultrasonic sound, 2) the difference of the distance between the locations of the activation for the stimuli and the sensor, 3) the effect of overlap of the multiple responses for the plural pitch perceived for ultrasonic bone-conducted stimuli [9], that could be accounted for by the longer rise/fall time of the response peak observed shown at figure 2a and 2b.

As one of the interesting characteristics for bone-conducted ultrasound, we can perceive sharper directional sound image when stimulated by bone-conducted ultrasound than by bone-conducted audible sound. Although we expected that the ratios of the standardized mean intensity of the activity for the deviants to the standards for the ultrasonic stimuli would become larger than that for the audible stimuli, no significant difference was observed.

Acknowledgements

This work was supported by Grant-in-Aid (No.12470359) of Ministry of Education, Science, Sports and Culture of Japan and was also supported by grant E-CH980201, Electrotechnical Laboratory, Agency of Industrial Science and Technology, Ministry of International Trade and Industry, Japan, and was partly supported by Kyowa Electronic Industry Co., Ltd.

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